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THOMAS M. HILLS, Ph.B. (Wooster), and a recent graduate student in the University of Chicago, has been appointed assistant professor of geology in the Ohio State University.

CHARLES B. WILSON, Ph.D. (Hopkins), has been appointed professor of biology at the State Normal School, Westfield, Mass.

DISCUSSION AND CORRESPONDENCE

AMOEBA MELEAGRIDIS

TO THE EDITOR OF SCIENCE: Nearly two years ago there appeared in this journal a communication by Drs. L. J. Cole and P. B. Hadley,¹ concerning the etiology of a protozoan disease of turkeys which demands some notice on my part.

The disease in question was investigated by me in 1894 and described in detail in a bulletin of the Bureau of Animal Industry, U. S. Department of Agriculture which was published in 1895. The disease is confined to the two cæca and the liver. Minute round bodies not more than 8-12 μ in diameter appear in enormous numbers in the submucous and intramuscular tissue of the walls of the cæca and may extend even beyond these to the mesenteries. In the liver there are circular spots, representing partial necrosis of the liver tissue and in these spots the same organisms are also present in great numbers. This parasite I assumed to be an amoeba and called it *A. meleagridis*. The analogy between it and human amœbiasis was very close.

In the communication of Drs. Cole and Hadley, my interpretation of the parasite is promptly disposed of and the latter stated to be a stage in the life history of the common coccidium of fowls and other domesticated and wild birds. This coccidium has been known since Rivolta first described it in 1878. Though I felt grave misgivings concerning the position taken by these writers, I nevertheless refrained from expressing my views until a full report should have appeared. In the meantime my patience has been tried by repeated iterations of the statements in various journals, scientific and practical, without any offer of proof that their position had any

basis in fact. At last two and a half years after their preliminary statement a bulletin² appears.

As an illustration of the way "facts" will grow when unchallenged I select the following statements from preliminary papers:

Since the investigations of Theobald Smith published in 1895 it has been commonly believed that the disease [blackhead] is due to an amoeba, *A. meleagridis* Smith. The present writers believe³ they have demonstrated, however, that the disease is caused by a coccidium which according to the nomenclature adopted may be a variety of *C. cuniculi* and that *A. meleagridis* is probably the schizont stage in the development of the coccidium.⁴

The discovery that the so-called blackhead of turkeys so common in this country is a form of coccidiosis (SCIENCE, 1908, N. S., XXVII., p. 994) and that the causative organism *C. cuniculi* is one of the most important factors in the causation of the so-called white diarrhœa of chicks and of some cases of roup in fowls, has called the attention of the student of protozoology in this country to the presence of a protozoan parasite whose ravages are annually costing the country hundreds of thousands of dollars.⁵

These excerpts speak for themselves. A "belief" becomes a "discovery" a year later, although no published data accompany the belief or precede the discovery. The discovery consists in fitting together two parasites both regarded as distinct for many years. Furthermore, the avian coccidium is identified with the rabbit coccidium without proof. It is made the "most important factor" of a diarrhœal disease of chicks and of roup in fowls, also without proof. Roup has defied many investigators and is due probably to an invisible virus.

The full report now before us confirms my suspicions that the demonstration and discovery represented merely an inference or hypothesis. Yet upon this the report is built as if it were an assured fact. Nothing whatever

² No. 141, Rhode Island Agric. Exp. Station.

³ Italics mine.

⁴ Cole and Hadley, SCIENCE, 1908, N. S., XXVII., p. 994.

⁵ Hadley in *Centralbl. f. Bakt., Erste Abth. Orig.*, 1909, 52, p. 147.

¹ 1908, N. S., Vol. XXVII., p. 994.

has been added to existing knowledge, and the expensive work done in the form of experiments is worthless to future investigators, because the authors have failed to keep apart ordinary coccidiosis and the parasite producing the specific cæcal and liver lesions. Even though subjectively convinced of the truth of their hypothesis, they should have objectively recorded the lesions and kinds of parasites found in the subjects of their experiments, so that others, who refuse to accept their hypothesis, might still have utilized the results. We have now a report which is neither one thing nor the other; it is neither on coccidiosis nor on entero-hepatitis.

When I first heard of entero-hepatitis as a "coccidiosis," I went over all the material from cases of the disease then in the laboratory to endeavor to read if possible this new hypothesis into the facts, although I had already stated in my early report (1895) that "it is very improbable that these bodies (coccidia) stand in any genetic relation to the true micro-parasite of the disease." This recent enquiry, however, carried me still farther away from this new hypothesis.

The weakness of the position taken by Cole and Hadley can be easily grasped by readers who are not protozoologists and pathologists when put in possession of a few fundamental facts. It has been the experience of microbiologists for the past thirty years that when a disease which is apparently due to a certain causative organism shows now one type of lesion, now another, now the presence of the suspected organism, now its absence, two infectious agents are involved which may work together or separately.

Whenever microorganisms can not be studied in pure culture artificially the infection with the products of disease may lead to double or even triple infections, because two or even three parasites may be in the infecting material. The same may occur spontaneously in any restricted territory where several diseases have coexisted for years. Most animals living in such locality may become the victims of several diseases. The only way out of the difficulty is to study the disease as it occurs in widely separated localities. If it

can be shown that outbreaks of entero-hepatitis may occur without coccidia and that outbreaks of coccidiosis may occur without liver disease and the presence of *A. meleagridis*, we have cleared away most of the difficulties surrounding the interpretation of a dual infection. Let us see what facts we can bring together bearing on this phase of the subject.

In 1894 I examined animals from nineteen farms, but only on two was coccidiosis present. This spring I examined a small flock of young turkeys kindly incubated and reared for me by Dr. Austin Peters. Though six out of nine of this flock died of "blackhead," without being exposed to any disease so far as we can discover, *not a single coccidium* was found either in the diseased or in the healthy animals. By a stretch of imagination it might be claimed that coccidia had not time to mature in these animals, which either died or were killed in from four to ten weeks after hatching. But as I have seen mature coccidia cysts in turkeys four weeks old this argument can not be used.

Although avian coccidiosis has been known since 1878, it is strange that close observers like Rivolta and many subsequent writers fail to report lesions of the liver which are so characteristic of the entero-hepatitis of turkeys. Surely this striking lesion would not have escaped even the most cursory and superficial examination. The authors in their recent report fail to distinguish between coccidiosis of the liver in which the epithelium of the bile ducts is the seat of the invasion, and the embolic, blood infection of the turkey's liver in which the parenchyma alone is affected. I do not recall any description of either type of liver disease in the coccidiosis in birds, although there is no reason why liver coccidiosis might not be found in birds as in rabbits. Leaving, however, aside this important distinction, let us see what the authors say of "coccidiosis" in other birds (on page 180 of their recent report). In four guinea-fowls, coccidia were present in either intestines or cæca, *but there were no liver lesions.*^{*} In two out of five ducks, coccidia were present in the cæca *but not in the liver.*
^{*}Italics mine.

Three pheasants were infected with coccidia but the livers are not mentioned. In two quail the typical lesions of blackhead were present in intestines and liver, the organism being found both in the *tissues* (?) and the intestinal contents. In one grouse coccidia were found. The liver is not mentioned.

Of seventeen pigeons all of which died, some with symptoms of coccidiosis, the organisms were found in nine and were usually accompanied by such lesions of either intestines or liver that a diagnosis of coccidiosis was justifiable. In several of the other eight pigeons, lesions which resembled those of *blackhead* were found both in intestines and liver, but apparently *not accompanied by coccidia*.

Sjöbring,⁷ who studied coccidiosis among birds in Sweden, describes forms belonging to two genera of coccidia. The one, evidently the predominating if not the only one observed by Cole and Hadley and by me, was found by Sjöbring in pheasants. The other, characterized by the presence of two instead of four spores, was encountered in many different species of birds. The author states distinctly that he found neither kind in the liver.

Since the writer's work in 1894 the enterohepatitis of turkeys has been encountered in the common fowl. It seems as if this parasite of turkeys had adapted itself to fowls and to other species of birds. In the above quotations from Cole and Hadley's work we see enough uncertainty to make us believe that the authors saw now one disease, now the other, now both together in different birds without distinguishing between them.

There is thus ample evidence to show that enterohepatitis may run its course in a flock without the presence of a single coccidium cyst to suggest coccidiosis. On the other hand, it is evident that coccidiosis among birds has been frequently seen during the past thirty years, but without involvement of the liver. Finally a double infection seems to have been the rule at the Rhode Island Experiment Station, where the work of Cole and Hadley was done and where the animals used in the experiments were reared.

⁷ *Centralbl. f. Bakt., Erste Abth.*, 1897, 22, p. 675.

This simple fundamental statement must suffice for the present. Aside from this there are many reasons why *A. meleagridis* and *C. tenellum* should not be regarded as identical. The former organism has no morphological characters which even remotely suggest a coccidium, and its situation and mode of attack upon the tissues are likewise wholly different from those which accompany coccidiosis. To state more than this would require a minute analysis of many pages of text in which the writers have laboriously endeavored to explain why true coccidia are met in some cases and not in others. If we should try to describe kangaroos and zebras intermingling in an enclosure, now in terms of one, now in terms of the other by assuming a genetic relationship between them, we would be in the same predicament in which the authors find themselves. To attempt to correct matters would be impossible.

It is obvious that in pathological work it is important to distinguish between lesions of different character, for they are of great service in the study of causation. In biological research it is far more important to keep morphological entities apart than to throw them together, unless very good reasons appear for identifying them. It is always possible for our successors to put them together, whereas a separation is impossible when a single term such as "blackhead" or coccidiosis is used to cover all. Rivolta had the same problem before him when first describing avian coccidiosis.⁸

In 1873 he noticed in the intestinal wall of fowls, dead of disease or killed, white points, the size of a poppy seed, found in the submucous connective tissue. These were small cysts full of "navicellæ" (merozoites?). In 1878 he saw in young chickens a disease, characterized by emaciation, diarrhoea, pallid flesh, etc., and by the presence of large numbers of minute white points in the duodenum. They appeared to be in the submucosa. In the intestinal contents many oval psorosperms (coccidia cysts?) were found. Rivolta

⁸ "Della gregarinosi dei polli, etc.," *Giorn. di anat. fisiol. et patol. degli animali*, Pisa, 1878, X., p. 220.

rejects the identity of submucous cysts and psorosperms for the following reasons:

1. The psorosperms always inhabited the epithelial cells, the gregarines the submucous connective tissue.

2. There were fowls which contain thousands of psorosperms but no gregarines.

3. There were found young chickens, black-birds and crows with gregarinosis without showing any psorosperms.

Rivolta's example might well be followed by our younger scientists. It is easier for the time being to make all forms over into a single species but in the end it is likely to lead to nothing. Rivolta, by the way, says nothing of liver lesions.

Another instance of the possible presence of two distinct parasites constituting what has for eighteen years been regarded as one, has recently been discussed by A. Theiler.⁹ Theiler thinks that what has hitherto been regarded as a single blood corpuscle parasite in Texas cattle fever represents two. In the first report¹⁰ on this disease both forms were shown to appear in the blood of cattle which had received a single injection of blood from a southern animal. Both live within the red cells, one type appearing first in the course of the disease, then the other. Theiler argues with much force that there are two species involved because in some parts of the world one type alone was reported as present in the blood of diseased animals, in other parts, the other type. In our own country both types occur. Without accepting for the moment Theiler's views, which I have not yet studied in detail, I think they are suggestive and worth careful attention. Fortunately in our report these types have been noted separately in the protocols, so that even after eighteen years the records are available for an analysis of Theiler's position.

Among the other blemishes of a work which otherwise shows much industry and study and a commendable care in editing is the use of the term *Coccidium cuniculi* and the suggestion

that there is any direct relation between the coccidium of the rabbit and that of birds. To assume that a species which refuses to invade near mammalian relatives and which seems to cling to the rabbit host throughout the world should have a closer relationship or even be identical with the avian coccidium seems to be attributing to nature a fickleness which students of parasitism know only too well does not exist. So clearly defined and narrow is the range of parasites even in the same host that it is with difficulty that coccidia locate in the epithelium of the large intestine when the epithelium of the upper small intestine has been preempted. The statement should therefore have been based on some actual experiments on birds with *C. cuniculi* of the rabbit.

In order to avoid misunderstanding in making this criticism, I wish to state emphatically that I do not regard my early work as in any sense complete. The questions concerning the amoebic character¹¹ of the bodies I described, the simple or complex nature of their life cycle, the direct, indirect or intermediate mode of infection do not come into consideration. Whatever position concerning one and all of them I had taken may be disputed as long as the life cycle has not been satisfactorily worked out. The final solution of these questions can be reached only after years of experimental breeding and rearing in carefully guarded territories on which no poultry is kept and from which even game and other wild birds are excluded. My criticism is confined to the confusing of an old well-known with a new and poorly known protozoan parasite and the consequent uselessness of the investigation as a basis for further work. I also wish to protest against the publication of premature, undigested, controversial statements in the form of preliminary notices years before the appearance in print of the actual work on which such statements are presumably based.

THEOBALD SMITH

HARVARD MEDICAL SCHOOL,
September 20, 1910

⁹ *Ztschr. f. Infektionskrankheiten d. Haustiere*, etc., 1910, 8, p. 39.

¹⁰ Smith and Kilborne, "Investigations into the Etiology of Texas or Southern Cattle Fever," Washington, 1893.

¹¹ Amoebic changes in form have been noted recently in liver tissue examined immediately after chloroforming affected turkeys.